

CLAIMS:

- Sub A4*
- 1- A method to achieve MHC-class II mediated immunomodulation in a mammal in need of such treatment, which comprises administering to the mammal at least one statin, or a functionally or structurally equivalent molecule, in an amount effective to modulate MHC class II expression in the mammal.
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- 2- A method to achieve MHC-class II mediated immunosuppression in a mammal in need of such treatment, which comprises administering to the mammal at least one statin, or a functionally or structurally equivalent molecule, in an amount effective to suppress MHC class II expression in the mammal.
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- 3- A method to achieve MHC-class II mediated anti-inflammatory effect in a mammal in need of such treatment, which comprises administering to the mammal at least one statin, or a functionally or structurally equivalent molecule, in an amount effective to suppress MHC class II expression in the mammal.
- 4- The method of claims 1, 2 or 3, wherein said mammal is a human.
- Sub B2*
- 5- The method of claims 1, 2 or 3, wherein said mammal does not suffer from hypercholesterolaemia.
- 6- The method of claims 1, 2 or 3, wherein said amount is effective to specifically modulate IFN- γ inducible MHC class II expression.
- 7- The method of claims 1, 2 or 3, wherein said mammal is suffering from a condition which involves IFN- γ inducible CIITA expression.
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- 8- The method of claims 1, 2 or 3, wherein said mammal is suffering from a condition which is an autoimmune disease.
- 9- The method of claim 8, wherein said autoimmune disease is type I diabetes, multiple sclerosis or rheumatoid arthritis.

10- The method of claims 1, 2 or 3, wherein said mammal is under treatment in preparation of or after an organ or tissue transplantation.

11- The method of claims 1, 2 or 3, wherein said mammal is suffering from a condition which is psoriasis or inflammation.

5 12- The method of claim 3, wherein said mammal is suffering from a dermatological condition and said statin is used in a topical application.

13- The method of claims 1, 2 or 3, wherein said statin is Compactin, Atorvastatin, Lovastatin, Pravastatin, Fluvastatin, Mevastatin, Cerivastatin, or Simvastatin.

10 14- The method of claims 1, 2 or 3, wherein said statin, or said functionally or structurally equivalent molecule, has no lipid-lowering effect.

15 15- The method of claims 1, 2 or 3, wherein the statin, or a functionally or structurally equivalent molecule, is administered in the absence of any other immunosuppressive agents.

16- The method of claims 1, 2 or 3, wherein said amount is comprised between 10 and 80 mg per day.

17- The method of claims 1, 2 or 3, wherein said amount is comprised between 20 and 40 mg per day.

18- The method of claims 1, 2 or 3, wherein said administration comprises intralesional, intraperitoneal, intramuscular or intravenous injection; infusion; or topical, nasal, oral, ocular or otic delivery.

19- The method of claims 1, 2 or 3, wherein said administration is made daily.

20- The method of claim 2 or 3, wherein the immunosuppression or anti-inflammatory effect is the result of repression of T lymphocyte activation.

- 21- A process for regulating IFN- γ -induced CIITA expression, and CIITA-dependant inter- or intra-cellular events, said process comprising the step of contacting an IFN- γ responsive cell with at least one statin or at least one functionally or structurally equivalent molecule.
- 22- The process according to claim 21, wherein said contacting is carried out *in vivo* or *in vitro*.
- 5 23- The process according to claim 21, wherein said statins are Compactin, Atorvastatin, Lovastatin, Pravastatin, Fluvastatin, Mevastatin, Cerivastatin or Simvastatin.
- 24- The process according to claim 21, wherein said IFN- γ responsive cell is a cell which has the capacity to become MHC-II positive on induction by IFN- γ .
- 10 25- The process according to claim 24, wherein said cell is a primary human endothelial cell, a primary human smooth muscle cell, a fibroblast, a monocyte-macrophage, a cell of the central nervous system, a ThP1 cell, a melanoma cell or a Hela cell.
- 26- The process according to claim 21, wherein the regulation of IFN- γ -induced CIITA expression is an inhibition of this expression.
- 15 27- The process according to claim 21, wherein the regulation of IFN- γ -induced CIITA expression is solely achieved by inhibition of the CIITA inducible promoter IV.
- 28- The process according to claim 21, wherein said intracellular events comprise induction of MHC-II expression by IFN- γ .
- 29- The process according to claim 28, wherein the regulation of CIITA expression generates a quantitative regulation of MHC-II expression.
- 20 30- The process according to claim 21, wherein said intercellular events comprise MHC-II-mediated T cell activation and proliferation.
- 31- The process according to claim 21, wherein said regulation can be reversed by addition of L-mevalonate.
- 25 32- The process according to claim 21, wherein said regulation of CIITA expression by said inhibitor is dose dependant.

33- A method for identifying molecules that inhibit IFN- γ induced CIITA expression, said inhibition being at least partially reversible by addition of L-mevalonate, comprising the steps of:

5 -contacting a cell which is IFN- γ responsive with a candidate inhibitory molecule and with IFN- γ ;

 -detecting the inhibition or absence of MHC class II expression in the presence of the candidate molecule;

 -further contacting the cell with L-mevalonate; and

 -detecting a total or partial reversal of the inhibitory effect.

10 34- A method for identifying molecules that inhibit IFN- γ induced CIITA expression, comprising the steps of:

 -contacting a cell which is IFN- γ responsive with a statin, or a functional or structural equivalent thereof, and with IFN- γ ;

15 -detecting the inhibition or absence of MHC class II expression in the presence of the statin, or the functional or structural equivalent thereof.

35- A method of treating a patient afflicted with an autoimmune disease, comprising administering to said patient a compound that inhibits 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA reductase) in an amount effective to treat said disease:

20 36- The method of claim 35 wherein said compound has a therapeutically insignificant lipid-lowering effect and suppresses MHC Class II expression.

37- A method of treating a patient suffering from an autoimmune disease or condition comprising:

 administering to said patient at least one compound, capable of measurable HMG-CoA reductase inhibition and inhibition of MHC Class II expression in said patient, in an amount effective to treat such autoimmune disease or condition.

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38- A method of treating a patient in preparation for or after an organ tissue transplant comprising:

5 administering to said patient at least one compound capable of measurable HMG-CoA reductase inhibition and inhibition of MHC Class II expression in said patient, in an amount which is effective to prevent tissue rejection.

39- A method of preventing or treating tissue or organ rejection in a patient comprising administering to said patient a compound that inhibits 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase) in an amount effective to prevent or treat tissue or organ rejection.

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